

**UNITED STATES DEPARTMENT OF COMMERCE****United States Patent and Trademark Office**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/360,934 07/26/99 COVACCI

A CHIR-0158

EXAMINER

HM22/0410

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ART UNIT	PAPER NUMBER

1638

DATE MAILED:

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04/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.
09/360,934

Applicant(s)

Covaccl et al.

Examiner

Phuong Bul

Group Art Unit
1638



THE PERIOD FOR RESPONSE: [check only a) or b)]

- a) ☒ expires 4 months from the mailing date of the final rejection.
- b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

- ☐ Appellant's Brief is due two months from the date of the Notice of Appeal filed on _____ (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Mar 12, 2001 has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

- ☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.
- ☐ will not be entered because:
- ☐ they raise new issues that would require further consideration and/or search. (See note below).
 - ☐ they raise the issue of new matter. (See note below).
 - ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
 - ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☒ Applicant's response has overcome the following rejection(s):

The 35 USC 112, 2nd paragraph rejection of claims 39, 40, 42, 43, 45, 46, 48-50, and 52.

- ☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:

See attached sheets.

- ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: 38-40 and 42

Claims objected to: None

Claims rejected: 43, 45, 46, and 48-53

- ☐ The proposed drawing correction filed on _____ ☐ has ☐ has not been approved by the Examiner.
- ☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Other

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DETAILED ACTION

1. The Office acknowledges the receipt of applicant's after-final amendment D, Paper No. 15, and the executed declaration of Giuseppe Del Giudice under 37 C.F.R. 1.132. The amendment will be entered upon the filing of an appeal. Accordingly, new claim 53 will be entered. Claims 38-40, and 42-53 are pending and are examined in the instant application.

35 U.S.C. 112, second paragraph

2. The rejection of claims 39, 40, 42, 43, 45, 46, 48-50, and 52 under 35 U.S.C. 112, second paragraph, as set forth in the previous Office action has been obviated by applicant's amendment to the claims. Accordingly, this rejection is hereby **withdrawn**.

35 U.S.C. 112, first paragraph

3. The rejection of claims 43, 45, 46, 48-52 and new claim 53 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *H.pylori* cytotoxin and non-toxic immunogenic fragments thereof, does not reasonably provide enablement for "prophylactic or therapeutic vaccine" recitation in the claims, nor methods for making and using this vaccine, as set forth in the previous Office action, Paper No. 3, mailed February 7, 2000, is hereby **maintained**.

Receipt is acknowledged of the signed copy of the Declaration of Giuseppe Del Giudice under 37 C.F.R. 1.132.

Applicant's traversal of this rejection has been fully considered, but was not found persuasive. Applicant asserts that it would be routine to one of ordinary skill in the art to test the

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candidate vaccines claimed for vaccine efficacy since there existed at the time of the invention, animal models for the study of *H.pylori* infection. However, this is not the real issue with regard to the lack of enablement of applicant's claimed prophylactic compositions and methods. The real issue is whether one skilled in the art would doubt the efficacy of applicant's compositions for the prophylactic treatment of *H.pylori* infection. For many infectious diseases, animal models exist just as in this case. However, the mere existence of an animal model does not immediately enable all candidate vaccines. Otherwise, there would really be no need for animal models in the first instance. The existence of an animal model merely provides a tool which can be used for assessing whether or not a vaccine candidate does or does not work. Animal models do not, of themselves, increase the chances that a particular vaccine candidate will work. To expect otherwise would be to say that any vaccine candidate developed for a disease for which there exists an acceptable animal model would inherently be enabled.

Turning then to the issue of enablement in its proper context, would one skilled in the art have doubted the enablement of any fragment of the *H.pylori* CT polypeptide of any length greater than or equal to 10 amino acids that both is non-toxic and induces antibodies to *H.pylori* for the protection against *H.pylori* infection? As indicated by applicant, the correct standard for evaluating enablement is set forth in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). In deciding whether or not a claim is enabled and the scope of that enablement, the standard requires that 8 factors be considered. It was against the backdrop of these factors that the discussion of Exhibit F (as correctly indicated by applicant) arose. The Office referred to the section of the Nedrud

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article to indicate that the mechanism of vaccine protection was not fully understood at the time of the instant invention. The Nedrud article sets forth evidence that T-cells may play a role in protection from *H.pylori* infection, thus supporting the position that merely establishing that a protein is immunogenic does not establish that the protein will be protective.

The Marschetti reference submitted by applicant has also been carefully considered. Initially, it should be noted that the mature CT protein, TOX100 is shown to be 33.3% protective when co-administered with a mucosal adjuvant. As previously indicated, use of a mucosal adjuvant is not contemplated by the instant disclosure. In Table 1 of this reference, the VacA protein is shown to be 23.1% protective without adjuvant and 75% and 79.7% protective with adjuvants. Thus, the use of an adjuvant significantly enhances a protective effect. The 33.3% protection for TOX100 with adjuvant then suggests that immunization of TOX100 would have been significantly less without an adjuvant. The claimed vaccine comprises a detoxified form of the CT protein which has not been shown to be protective. Moreover, the TOX37 and TOX 58 fragments did not provide protection. Though applicant characterizes Marschetti's criteria for evaluating protection as stringent, Marschetti is not actually requiring 100% protection. Instead, as set forth above, Marschetti allows that 33.3% of the subjects were protected against infection when immunized with TOX100. A criteria for protection in one subject evaluated by the absence of any colony forming units in the stomach of the vaccinated subject is appropriate. No other rational criteria has been offered by applicant, even though the instant specification uses the term "partial" in regard to protection. What exactly is "partial" protection and how is it evaluated? If

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a host has fewer colony forming units, yet still manifests the disease conditions attributable to *H. pylori* infection, would that host nonetheless be characterized as being partially protected? Finally, given the failure to achieve protection with two fragments, Marschetti supports the Office's position that the mere existence of acceptable animal models does not inherently enable a protein or its fragments as being protective.

4. Claims 38, 39, 40 and 42 are allowable. New claim 53 has been added to the 35 U.S.C. 112, first paragraph rejection as set forth above.

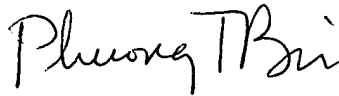
5. Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Bui whose telephone number is (703) 305-1996. The Examiner can normally be reached Monday-Friday from 6:30 AM - 4:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Phuong Bui
Patent Examiner
Group Art Unit 1638
April 3, 2001


PHUONG T. BUI
PRIMARY EXAMINER